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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/496,332	01/28/00	GORMAN	K

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EXAMINER	
GOLDBERG, J	
ART UNIT	**PAPER NUMBER**
1655	21

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/494,332	Applicant(s) GORMAN ET AL.	
	Examiner Jeanine A Enewold Goldberg	Art Unit 1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 August 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *25 and 46* is/are allowed.

6)☒ Claim(s) *1-24,26-31,33,35,37,39,41 and 43-45* is/are rejected.

7)☒ Claim(s) *32,34,36,38,40 and 42* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). *18* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to the papers filed August 27, 2001. Currently, claims 1-46 are pending. All arguments have been thoroughly reviewed but are deemed non-persuasive for the reasons which follow. This action is **FINAL**.

2. Any objections and rejections not reiterated below are hereby withdrawn.

Maintained Rejections

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 1-15 and 43-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Han et al (PNAS, Vol. 88, pg. 1711-1715, March 1991) or Maertens et al (US Pat. 5,846,704, December 1998).and Backus et al (US Pat 6,001,558, December 1999) in view of Nedjar et al (J. of Virological Methods, Vol. 35, No. 3, pg 297-304).

Han et al. (herein referred to as Han) teaches the sequence of 341 base pairs from the 5' untranslated region (UTR) of HCV and alignment of this sequence from several different HCV isolates. Han teaches extracting the plasma from HCV-positive or negative blood donors. RNA was isolated and converted into single-stranded cDNA by

reverse trancriptase using the appropriate cDNA primer (pg 1711, col 2). Han teaches primers for the PCR amplification of 5' UTR and means of cloning these PCR products (pg. 1711, col. 2, and Figure 2). The PCR products were analyzed by southern blot hybridization using a labeled oligonucleotide probe (pg 1711, col 2). Han teaches that when the sequence of the 5' UTR is compared among isolates, there is a high degree of sequence homology and that the sequence mismatches that are present are clustered in 5 positions, as taught in Figure 2 (see also pg. 1713, para 1). Han teaches that the 342 base pair 5' UTR sequence represents a signature sequence that could serve as a HCV-specific DNA probe for the detection of all strains of the virus and further that the primers and highly reliable PCR protocol method as taught could be used for this purpose (pg 1714, para 4).

Maertens et al (US Pat. 5,846,704, December 8, 1998) teaches a method of genotyping of HCV isolates using probes targeting sequences from the 5' UTR region of HCV (abstract). Maertens teaches extracting viral DNA from serum such that RNA was pelleted (col 24, lines 60-68). Random primers were then added such that cDNA was synthesized (col 24, lines 60-68). Maertens teaches amplifying the cDNA with outer primers and subsequently inner primers (col. 25, lines 5-10). The PCR product was then subjected to electrophoresis in an agarose gel and ethidium bromide staining (col. 25, lines 14-15). Furthermore, strips of immobilized HCV-specific primers developed and hybridized with PCR amplified DNA fragments of the 5' UTR for visualization (col. 25, lines 50-60). Maertens teaches a kit which comprises a set of primers, a set of probes immobilized on a solid substrate, and buffers (col. 20, lines 45-55). Maertens

provides specific primers for each of the isolates and universal primers which may be used (Table 4 and 5). SEQ ID NO: 1 of the instant application overlaps SEQ ID NO: 27 of Maertens. Nucleotides 17-25 of the instant application are identical to nucleotides 1-9 of Maertens. SEQ ID NO: 2 of the instant application overlaps SEQ ID NO: 4 of Maertens. Nucleotides 5-25 of the instant application are identical to nucleotides 1-20 of Maertens.

Backus et al. (herein referred to as Backus) teaches amplification and detection of HIV-1 and HIV-2. Backus teaches oligonucleotides which amplify HIV-1 nucleic acids including oligonucleotides which are SEQ ID NO: 3 and 5. Backus also teaches an oligonucleotide which comprises the nucleotides of SEQ ID NO: 4. Backus, furthermore, teaches oligonucleotides which amplify HIV-2 nucleic acids including oligonucleotides which are SEQ ID NO: 6 and 7. Backus also teaches oligonucleotide probes of SEQ ID NO: 13, 14 and 16 for HIV-1 and HIV-2. The primers chosen were from identified highly conserved sequence regions (col. 10, lines 50-60). Backus teaches that a biological sample is used which included cellular-or viral material, hair, body fluids, or cellular material containing nucleic acids which may be detected (limitations of Claims 8 and 23).

Han and Backus do not specifically teach co-amplifying or co-detecting HCV and HIV using the primers of the instant claimed invention.

However Nedjar teaches a method of co-amplification of specific sequences of HCV and HIV by using PCR assays. Nedjar teaches that primer pairs from HCV and HIV-1 sequences were used (pg 299). Nedjar teaches the conditions of the multiplex

reaction. Nedjar teaches the ability to co-amplify specific sequence from two different viral genomes in the same reaction mixture offers the possibility of simultaneous detection and diagnosis of more than one viral agent in serum samples of infected individuals.

Further, in the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the court determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologues, however, the court stated

> "Normally, a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologues because homologues often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties."

Since the claimed oligonucleotides simply represent structural homologues of the full length disclosed 5' UTR HCV and the HIV-1/2 sequence concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers and probes are *prima facie* obvious over the cited reference in the absence of secondary considerations. Therefore, it would have been **prima facie** obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Han and Backus in view of Nedjar to obtain the claimed invention as a whole. The skilled artisan would have been motivated to have used primers from the 5' UTR region to detect HCV, as taught by Han and primers from HIV-1 and HIV-2 as taught by Backus. Since Han provides an alignment of several

isolates which show conserved regions between the isolates, and delineates the ORFs, the ordinary artisan would have been motivated to have designed primers which amplify various regions of interest from the 5' UTR region. Specifically, the skilled artisan would have chosen SEQ ID NO: 1 and 2, which flank ORF3. Furthermore, the skilled artisan would have chosen SEQ ID NO: 11, 12 or 13 for probing the detection of HCV. The ordinary artisan would have been motivated to amplify the 5' UTR region of HCV since Han teaches that the 342 base pair 5' UTR sequence represents a signature sequence that could serve as a HCV-specific DNA probe for the detection of all strains of the virus and further that the primers and highly reliable PCR protocol method as taught could be used for this purpose. The ordinary artisan would have used the probes and primers from Backus, based upon the detailed analysis provided that these probes and primers were for conserved regions among the numerous isolates. The ordinary artisan would have combined the teachings of Han and Backus in view of Nedjar for the express benefit of diagnosing more than one viral agent in samples of infected individuals. The ordinary artisan would have recognized that the detection of more than one viral agent would have been ideal for saving time, and reagents. The multiplexing of numerous primers into a single reaction has the express benefit of saving reagent by limiting the number of assays and also saving time of scientists since the results may be obtained simultaneously. Thus, the ordinary artisan would have combined the teachings of detecting HCV with the teachings of detecting HIV-1 and HIV-2.

Response to Arguments

The response traverses the rejection.

The response asserts that "it is not sufficient to show that a skilled artisan might have a reasonable expectation of success in using either the particular HCV-specific primers or the particular HIV-specific primers of this invention. It must also be shown that a skilled artisan would reasonably expect that these particular primers can be used in combination to detect HCV and HIV nucleic acids in a sample". Applicants cite *In re Deuel, In re O'Farrell* and states that there is no reasonable expectation of success.

Applicant's cite a passage, in addition to the passage provided, in *Deuel* which is deemed to support applicant's position. The examiner agrees with the position that the Deuel court states "in all of these cases...the prior art teaches a specific, structurally-definable compound and the question becomes whether the prior art would have suggested making the specific molecular modifications necessary to achieve the claimed invention". However, the examiner also notes that Deuel teaches at 1215, col. 1, No. 7, "Further, while the general idea of the claimed molecules, their function, and their general chemical nature may have been obvious from Bohlen's teachings, and the knowledge that some gene existed may have been clear, the precise cDNA molecules of claims 5 and 7 would not have been obvious over the Bohlen reference because Bohlen teaches proteins, not the claimed or closely related cDNA molecules". In contrast, in the instant case, the very source of the claimed nucleic acid was provided. The reference even directs the attention to the very region the oligonucleotides are pulled from. Deuel did not find it obvious to probe a library to find full length DNA molecules given a smaller portion of the molecule. The instant case, however, is directed to a known full length molecule and determining smaller molecules which may

function as probes and/or primers. Thus, the normal circumstances for a prima facie case should be followed as set out on 1214, col. 2. Han and Maertens teaches the full length 5'UTR region of HCV with specific probes and primers within the nucleic acid. Backus teaches probes and primer which either consist of the instant SEQ ID NO:s 3, 5-7, 13-14, and16 or comprise SEQ ID NO: 4.

Applicant then argues that there is no reasonable expectation of success. The legal standard for "reasonable expectation of success" is provided by caselaw and is summarized in MPEP 2144.08, which notes "obviousness does not require absolute predictability, only a reasonable expectation of success; i.e. , a reasonable expectation of obtaining similar properties. See , e.g. , In re O'Farrell , 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988)." In this factual case, there is express suggestion in the prior art to select primers which hybridize to the 5' UTR of HCV for detection of the nucleic acid. Further, since the art teaches the SEQ ID NO: 3, 5-7, 13-14, 16 and a nucleic acid comprising SEQ ID NO: 4, the art has provided specific motivation and teachings to choose the probes and primers for the HIV-1 and HIV-2 detection. These probes and primers were used in a multiplex analysis of HIV-1 and HIV-2 detection, thus there is motivation to select these sequences for multiplex analysis. With respect to choosing primers for 5' HCV detection, the prior art disclosed numerous different primer sequences and teaches selection of primers or probes which detect the HCV 5' UTR. The prior art teaches the parameters (i.e. size, parameters, homology) necessary to vary to achieve specific probes, and the prior art successfully meets this test. This is

sufficient for a reasonable expectation of success. The MPEP cites In re O'Farrell, which notes regarding "obvious to try" at page 1682, that,

In some cases, what would have been "obvious to try" would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful. E.g ., In re Geiger , 815 F.2d at 688, 2 USPQ2d at 1278; Novo Industri A/S v. Travenol Laboratories, Inc ., 677 F.2d 1202, 1208, 215 USPQ 412, 417 (7th Cir. 1982); In re Yates , 663 F.2d 1054, 1057, 211 USPQ 1149, 1151 (CCPA 1981); In re Antonie , 559 F.2d at 621, 195 USPQ at 8-9. In others, what was "obvious to try" was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it. In re Dow Chemical Co ., 837 F.2d, 469, 473, 5 USPQ2d 1529, 1532 (Fed. Cir. 1985); Hybritech, Inc. v. Monoclonal Antibodies, Inc .; 802 F.2d 1367, 1380, 231 USPQ 81, 90-91 (Fed. Cir. 1 986), cert. denied , 107 S.Ct. 1606 (1987); In re Tomlinson ; 363 F.2d 928, 931, 150 USPQ 623, 626 (CCPA 1966).

The court in O'Farrell then, affirming the rejection, notes " Neither of these situations applies here." For the instant case, it is clear that neither situations applies here either. For the 5' UTR primers, this is not a situation where the prior art fails to identify critical parameters since the prior art provides the parameters necessary for primer selection, including preferred sequence regions (see Figure 2 of Han et al, and

Table 4 and 5 of Maertens), the entire sequence at issue (see Figure 2 of Han), and a variety of particular functional species. Therefore, the prior art provides the information necessary to select probes and primers and the prior art would expect that every species selected in this manner would function in a detection assay. This is also not a situation where only general guidance was given. The prior art provides specific guidance regarding the use of primers and probes from this region of the HCV genome for detection purposes. With respect to the HIV-1 and HIV-2 probes and primers, Backus teaches SEQ ID NO: 3, 5-7, 13-14, 16 of the instant application and a nucleic acid comprising SEQ ID NO: 4 of the instant application. The art has provided specific motivation and teachings to choose the probes and primers for the HIV-1 and HIV-2 detection. Therefore, properly applying O'Farrell, it is not simply obvious to try to make the claimed invention, there is a reasonable expectation of success.

With respect to the experimentation required to determine which of those primers, may be successfully combined to multiplex HCV and/or HIV, the art has provided guidance with respect to the critical conditions required. Applciant's asserts that "the skilled artisan must therefore reasonably expect success from the recited sets of oligonucleotide primer without having to engage in any experimentation (routine or otherwise) to identify particular oligonucleotide set that would be suitable for the claimed multiplex PCR assay(s)" (pg 18 of the response filed August 27, 2001). This argument has been reviewed but is not convincing because the probes and primers would be expected to function in detecting the respective sequences. Thus, combining the sequences into a multiplex with the guidance in the art and motivation in the art would

be routine optimization which would constitute reasonable expectation of success. There is no requirement for absolute predictability. It is unclear what applicants are relying upon to make the statement that "the skilled artisan must therefore reasonably expect success from the recited sets of oligonucleotide primer without having to engage in any experimentation (routine or otherwise) to identify particular oligonucleotide set that would be suitable for the claimed multiplex PCR assay(s)".

The applicant's further argue there is not any such reasonable expectation of success. Applicant's argument directed to there is no reasonable expectation of success is apparently supported by Ausubel. The response provides Chapter 15.1 from Current Protocols in Molecular Biology as support that primer selection is "the factor that is least predictable and most difficult to trouble shoot. Simply put, some primers just do not work". This argument has been reviewed but is not convincing because primer selection is routine in the art at the time the invention was made. While this reference does teach that primer selection is the least predictable, the reference specifically provides "to maximize the probability that a given primer pair will work, pay attention to the following parameters..". Thus, the art provides guidance for the optimization of primers. Design of primer pairs is routine in the art and merely constitutes optimization which is well within the scope of the ordinary artisan. Moreover, specific optimization kits, computer programs and such are provided to aid the artisan in the primer selection. For example, computer programs exist which allow user input for primer selection parameters (see Nucleic Acids Research, 1994). The response asserts that the computers are also not foolproof, however, foolproof is not the standard to be met. As

stated in O'Farrell, "obviousness does not require absolute predictability of success. Indeed, for many inventions that seem quite obvious, there is no absolute predictability of success until the invention is reduced to practice. There is always at least a possibility of unexpected results, that would then provide an objective basis for showing that the invention, although apparently obvious, was in law non-obvious". Thus, absolute predictability is not required. The art provides the full length sequence of the 5'UTR of HCV and the specific probes and primers for HIV, the regions of interest and the approximate size of oligonucleotides to select from this region for detection of the region. Further, optimization of primers and primer pairs is routine in the art. The art teaches how to alter the conditions to obtain primer/primer pairs which amplify the target. As noted in *In re Aller*, 105 USPQ 233 at 235, "More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." Routine optimization is not considered inventive and no evidence has been presented that the probe selection performed was other than routine, that the products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art.

Applicant's further assert that the "skilled artisan must not only reasonably expect that the recited oligonucleotide primers will separately amplify HCV and/or HIV target sequences. He or she must also reasonably expect that these primer can successfully amplify for those sequences in a multiplex PCR assay". This argument has been reviewed but is not convincing because the individual primers for HCV and HIV are

expected to separately detect the HCV and HIV sequences respectively, especially the HIV sequences since they are taught to detect HIV. Once the primers are selected the art provides guidance to optimizing the conditions. Applicant's assert that Kimpton does not teach varying the primers, however, the examiner is not relying upon Kimpton to teach varying the primers, but rather the parameters of the reaction such as concentrations of the buffer, primers triphosphates, template, and polymerase, the number of cycles.

Applicants argue that "empirical testing and a trial-and-error approach have been used when testing primer pairs, because there is no means to predict the performance characteristics of a selected primer pair even among those that satisfy the general parameters of primer design". This argument has been reviewed but is not convincing because the requirement for predictability does not require absolute predictability. The art teaches numerous parameters to vary which allow optimization.

4. Claims 31, 33, 35, 37, 39, 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Han et al (PNAS, Vol. 88, pg. 1711-1715, March 1991) or Maertens et al (US Pat. 5,846,704, December 1998).and/or Backus et al (US Pat 6,001,558, December 1999) in view of Nedjar et al (J. of Virological Methods, Vol 35, No. 3, pg 297-304) as applied to Claim 1, 3-13, 40-44 above, and further in view of Ahern (www.thescientist.library.upenn.edu/yr1995/july/tools_950724.htlm, December 22, 1998).

Neither Han, Maertens, Backus nor Nedjar specifically teaches packaging necessary reagents into a kit.

However, Ahern teaches reagent kits offer scientists good return on investment. Ahern teaches kits save time and money because the kits already comes prepared.

Therefore, it would have been **prima facie** obvious to one of ordinary skill in the art at the time the invention was made to have modified the teachings of Han, Maertens and Backus in view of Nedjar with the teachings of Ahern to incorporate the necessary reagents into a packaged kit. The ordinary artisan would have been motivated to have packaged the primers, probes, and reagents of Han, Maertens and Backus into a kit, as taught by Ahern for the express purpose of saving time and money.

Response to Arguments

The response traverses the rejection. The response asserts that Ahern does not overcome any of Han's, Maertens', Backus', or Nedjar's deficiencies. Specifically the response asserts that Ahern does not teach or suggest any prepackaged PCR kit and specifically not a kit containing the particular probes and primers of the instant invention. This argument has been reviewed but is not convincing because the teachings of Ahern specifically teach packaging reagents necessary for a reaction into a kit. Thus, the ordinary artisan would have packaged the necessary reagents, primers, taught by Han or Maertens and/or Backus in view of Nedjar into a kit for all of the reasons of Ahern. Thus for the reasons above and those already of record, the rejection is maintained.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 1-15 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-64 of copending Application No. 09/493,353. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications are directed to a method of detecting HCV 5' UTR using SEQ ID NO: 1 and 2 of the instant application which are identical to SEQ ID NO: 2 and 7 of 09/493,353.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

The response traverses the rejection. The response asserts that upon allowable subject matter in the two cases, Applicant's agree to submit a terminal disclaimer. Thus for the reasons above and those already of record, the rejection is maintained.

Allowable Subject Matter

6. The instant IPC region and primers to the synthetic region are novel over the prior art. The SEQ ID NO: 8, 9 and 15 are not previously known in the art. However, Picone et al. (US Pat. 5,491,225, February 1996) and Blasczyk et al (Beitrage Zur Infusionstherapie Und Transfusionmedizin, Vol 34, pg 236-241, 1997-abstract only) teach incorporating IPC RNA into an assay. Picone et al. (herein referred to as Picone) teaches "internal positive control oligonucleotide sequences" are a recombinant or synthetic oligonucleotides that ensure assay users that the amplification process has occurred in the event that the sample being tested has no target nucleic acid. Additionally, Blasczyk et al. (herein referred to as Blascyzk) teaches a pair of primers which amplify a fragment of the human growth hormone gene was included as an internal positive amplification control. The presence or absence of specific PCR amplification allowed definite allele assignment without the need for any postamplification specificity step. Additionally, Blasczyk teaches that the internal positive control primers indicate a successful PCR amplification (abstract).

Thus, while the concept of internal control regions and primers to amplify are known in the art, the specific sequences of the instant used primers are novel.

Conclusion

7. **Claims 25, 46 are allowable over the prior art.** Claims **32, 34, 36, 38, 40, 42, are** objected to as being dependent upon a rejected base claim, but would be allowable

if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

8. Claims 1-24, 26-31, 33, 35, 37, 39, 41, 43-45 are not allowable.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Enewold Goldberg whose telephone number is (703) 306-5817. The examiner can normally be reached Monday-Thursday from 7:00AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax number for this Group is (703) 305- 3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jeanine Enewold Goldberg
September 10, 2001

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600

9/17/01